

Opportunities for Beryllium Health and Safety Research

<i>Specific Goal</i>	<i>Objective and Description</i>	<i>Direct Benefit</i>	<i>Est. \$M/Yr</i>	<i>Progress So Far</i>	<i>Needed Peer Review Expertise</i>	<i>Possible Interest (NNSA, EM, EH are DOE Offices)</i>	<i>Type of Research</i>
				Exposure	Total for Exposure		4.85
Improve sampling methods							
Fine particulates sampling							
Develop sampling methods that characterize fine and ultrafine beryllium particulate exposure.	Develop sampling methods for fine and ultrafine particulates that deposit in lungs. This item addresses a current worker safety issue. The method would allow researchers to determine the health risk of exposure to fine and ultrafine beryllium particles and allow practitioners to better monitor and control these exposures in the workplace.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	0.40	Size-selective samplers are available but require a personal, high-volume pump. This pump will require an intensive development effort.	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Applied
Develop sampling methods that characterize beryllium particulate exposure by mass, number, size fraction, chemical form, particle surface area.	Develop sampling methods that characterize beryllium particulate exposure by mass, number, size fraction, chemical form, particle surface area. This item addresses a current worker safety issue. The method would allow researchers to determine the health risk of exposure measured by various particulate parameters and allow practitioners to better monitor and control these exposures in the workplace.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	1.00	NIOSH completed basic analysis of particle agglomeration and surface areas.	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Applied

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							Applied
							Epi
							Basic
Real-time monitoring							
Develop promising near real-time monitoring instruments or sampling and analytical methods.	Develop promising intermediate-time, near real time, and real time (less than an hour to a few hours) monitoring instruments or sampling and analytical methods. These instruments and methods will improve worker and public protection, improve productivity through reduced production hold times and analytic costs, and reduce the cost of legacy and beryllium area cleaning and monitoring.	Identify and control exposures in the same shift that the exposure begins. Reduce analysis costs and hold times waiting for surface contamination sample results. Focus resources on controlling the greatest risks.	1.15	A number of methods are available; some at prototype stage. Final development to specified sensitivity, specificity, reliability, portability, etc., and validation, is needed. New methods may be needed for some situations, such as unique interferents.	Electrical and mechanical engineering, industrial hygiene, human factors, chemistry, instrument design, statistics, beryllium operations	NNSA, EH and NIOSH	Applied
Skin exposure							
Develop a method for quantifying skin and mucous membrane exposure.	The method would allow researchers to determine body surface exposures that are necessary to determine whether these exposures contribute to sensitization and disease. The method also would allow practitioners to better control these exposures.	Reduce risk of sensitization and disease.	0.50	Methods are available but need standardization and validation for beryllium.	Chemistry, industrial hygiene, statistics	NNSA, EH, and NIOSH	Applied
Uncommon surface sampling							
Develop standardized and validated sampling methods for uncommon surfaces and relevant media.	Develop standardized and validated sampling methods for general and porous surfaces, bulk samples, vacuuming, and other relevant media. Consistent and validated sampling methods for common as well as unusual types of surfaces will provide for better comparison of site conditions as they relate to beryllium exposure.	Improve consistency among sites on the validity of results and on identifying risks.	0.50	Methods are available but need standardization and validation for beryllium and for a variety of surface types.	Industrial hygiene, statistics, beryllium operations, chemistry	NNSA, EH, and NIOSH	Applied

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							Applied
							Epi
							Basic
Needed tools: Exposure							
Nanogram analysis							
Develop and validate analytic methods sensitive to the 0.1 nanogram per sample level of quantitation.	Develop and validate analytic methods sensitive to the 0.1 nanogram per sample level of quantitation. Methods also must speciate between beryllium, beryllium oxide, and various beryllium alloys.	Improve worker exposure characterization by lowering detectable limit on samples.	0.25	LLNL reports promising new technology using accelerator mass spectrometry for quantifying femptogram amounts of Be isotopes.	Chemistry, radiochemistry, nuclear physics, industrial hygiene, statistics	NNSA, EH, and NIOSH	Epidemiology
Particle reference materials							
Establish the availability of aerosol and particle standard reference materials.	Establish the availability of aerosol and particle standard reference materials. Similar to NIST standard reference materials. Various chemical forms, sizes, surface areas.	Needed to conduct research on improved sampling methods and beryllium toxicology in animal studies.	0.10		Metallurgy, industrial hygiene, statistics, particle physics, beryllium operations	NNSA, EH, and NIOSH	Epidemiology
Size-selective sampling							
Identify or develop a high-volume personal sampling pump.	Provide a high-volume personal sampling pump.	Improve worker exposure characterization by collecting detectable amounts of fine particulate .	0.10	Demand has some vendors developing prototypes.	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Applied

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							Applied
							Epi
							Basic
Use improved methods							
Different activities							
Determine the types of exposures that are generated by different types of activities.	Characterize the different types of exposures by concentrations in terms of mass, particle number, particle-size fractions, surface area, and chemical form.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	0.50	Limited progress with characterizing particle number exposure at Brush Wellman facilities.	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Epidemiology
Exposure correlates							
Determine which exposure parameters correlate with each other at different times and workplaces.	Determine which exposure parameters correlate with each other at different times and workplaces so that the most convenient parameter can be monitored, e.g., mass, number, size fraction, chemical form, particle surface area.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	0.25	A great deal of mass exposure data exists, and a very small amount of particle number exposure data exists.	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Epidemiology
Risk characterization							
Use of improved methods (e.g., sampling by mass, number, size fraction, chemical form, particle surface area and using real-time and nanogram analysis) to better characterize exposure risks in current DOE operations.	Use the improved methods to better characterize exposure risks in current DOE operations. Includes conducting more effective (focused on highest risks and more timely) sampling of current beryllium operations across the complex. The information will be used to understand if operations are being controlled adequately and which operations are of greatest concern.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	0.10	Size-selective samplers are available but require a personal, high-volume pump. This pump will require an intensive development effort.	Electrical and mechanical engineering, industrial hygiene, human factors, statistics, beryllium operations	NNSA, EH, and NIOSH	Applied

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							Applied
							Epi
							Basic
				Controls	Total for Controls		1.25
Develop improved controls.							
DOE-wide controls							
Develop improved engineering and administrative controls having DOE-wide application for beryllium operations, maintenance and construction activities.	Develop control technology for use by DOE complex. Document engineering controls and exposure data including efficiency and effectiveness. Operations that will benefit the most sites will be given preference. This item will provide better engineering controls for nonroutine operations. For instance, a vacuum cleaner designed to prevent release of contaminants during maintenance would significantly reduce the risk of exposure to maintenance personnel at virtually all DOE beryllium sites.	Reduce exposure risk, increase worker safety.	0.50	Efforts are ongoing but need dedicated resources and recognition to continue.	Beryllium operations, metallurgy, variety of engineering (i.e., electrical, mechanical, ventilation) industrial hygiene	NNSA, EH, and NIOSH	Applied
Develop a coating technology to mitigate particulate aerosol releases from surfaces.	This research aims to limit worker exposure by coating beryllium-containing or beryllium-contaminated items with a film that prevents beryllium release from the item. It will limit both inhalation and skin exposure. The result of this research will be a form of engineering control of skin exposure, which is preferable to the common administrative control of wearing gloves.	Increase worker safety and improve productivity by coating to reduce exposure and analysis costs and hold times needed to establish cleanliness.	0.25	Some technologies are available for general sealing and waste disposal, but they require validation. Other technologies may need to be developed.	Beryllium operations, metallurgy, coatings chemistry, industrial hygiene	EM and NNSA	Applied

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							Applied
							Epi
							Basic

Needed tools: Controls

Surface level risk

Determine the relationship between surface contamination and health risk.	This item will identify and/or develop models to determine the worker exposure that will result from various activities that disturb contamination on a surface. Existing models, e.g., for lead-contaminated dust in dwellings and radioactive particulates in DOE facilities, will be evaluated for relevance. The relevant existing or newly developed models will be validated for beryllium contamination. This effort will determine what, if any, surface levels constitutes a health risk.	Increase worker safety and provide the basis for health-based decisions for managing beryllium-contaminated items and spaces.	0.50	A few efforts failed to establish relationship. Additional effort is needed to either establish the relationship or validate that none exist.	Physics, statistics, industrial hygiene, occupational medicine	NNSA, EH, and NIOSH	Applied
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Health Effects

Total for Health Effects

8.50

Diagnosis

Disease in general public

Determine the prevalence of sensitization and disease in the public. Include support personnel around beryllium operations. Consider smoking. Include natural and other nonoccupational exposures.	This item will determine if individuals in the general population have sensitization or disease and if that correlates with ubiquitous sources of exposure, such as power plant fly ash or cigarette smoke. This will provide an understanding of the differences in worker occupational exposure versus ambient exposure to the general population and will allow for better deductive analysis of possible external sources when disease or sensitization is discovered, and a plausible work exposure cannot be found. Current data exists in several different programs both within and outside of DOE.	Provide basis for sound decisions for managing legacy issues and DOE groups with signs of disease but no plausible work exposure.	0.50	Will require large scope project involving other agencies and cooperation of private clinics. Some exposures to the general population are documented. Additional exposures need to be sought. Correlation of nonoccupational exposures to health effects	Occupational and public health epidemiology, industrial hygiene, statistics, environmental science, geology	EH and NIOSH	Epidemiology
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							Applied
							Epi
							Basic
Improved tests							
Develop and validate improved screening and diagnostic tests, including the identification of genetic factors that relate to risk.	Develop tests that are less invasive to perform, and more predictive of sensitization and disease, than the current tests. Prevent progression to disease. Develop screening tests that are better predictors of exposure, sensitization, and disease. Develop screening tests that are not based on cell proliferation (e.g., accelerator mass spectrometry analysis of specific proteins in blood).	Reduce uncertainty of diagnosis and thereby improve the quality of subsequent decisions. Improve prognosis of disease.	2.25	A potential improvement to the current screening test has been developed and needs validation. Other tests have yet to be developed. Very little recent progress has been made in therapeutic interventions or specific therapies.	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI, and NIOSH	Basic
Interventions and treatments							
Identify opportunities for therapeutic interventions (pre-CBD) or specific therapies for CBD.	This item is designed to develop new treatments for the disease that could slow or halt the disease process. Since death can occur in the mid-50's with quality of life issues resulting in the 40's, this would allow for patients to resume a more normal life and increase the life expectancy.	Improve quality of life for patients. Allow affected current workers to continue productive work for DOE. Minimize federal liability under EEOICPA.	0.75	Removal from exposure and steroid treatments are available but do not appear to help many patients.	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI, and NIOSH	Basic
Disease process.							
Dose-response							
Determine the dose-response relationship for beryllium sensitization and disease for different exposure parameters; i.e., mass, number, size fraction, chemical form, particle surface area.	Determine the dose-response relationship for beryllium sensitization and disease for different exposure parameters; i.e., mass, number, size fraction, chemical form, particle surface area.	Reduce exposure to airborne particulate posing greatest health risk. Focus resources on controlling the greatest risk.	0.75	A number of workplace and community epidemiology studies have been published. All suffer from weak exposure data.	Pulmonary medicine, statistics, epidemiology, industrial hygiene	EH , NHLBI, and NIOSH	Epidemiology

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							Applied
							Epi
							Basic
Natural history of disease							
Determine the natural history of beryllium disease: sensitization to disease; different rates of progression; workers and public; include nonoccupational exposures; risk factors; e.g., genetics, underlying disease, gender, age, smoking.	Determine timeframes of progression from initial exposure to disease using statistical analysis of existing clinical data. There are three groups of patients, those that do not progress in symptoms, those who progress but CBD is not the reason for death, and those who progress rapidly and die of CBD. The reason for the differences is unknown. This research will provide the knowledge needed for developing intervention and treatment options to reduce or eliminate disease progression.	Improve disease management. Intervene to minimize or prevent symptoms.	0.10	Some studies are completed but are for small populations. Some clinician experience is available but is not published. More and larger published studies are needed.	Pulmonary medicine, epidemiology, industrial hygiene	EH , NHLBI, and NIOSH	Epidemiology
Pharmacokinetic model							
Characterize and determine the health significance of the physiochemical properties of beryllium. Determine the bioavailability of beryllium at different locations in the body and the health impacts at those locations and on remote organ systems.	Develop and validate a pharmacokinetic model of beryllium in the body using both in-vitro and in-vivo techniques. The model will describe the body's immunological response to beryllium. It will include exposure to skin, mucous membrane and respiratory tract, as well as lungs. It will assist in confirming that beryllium is deposited in lungs, in determining the location of the deposits, and possibly identify the form of beryllium that is deposited. The model will assist in developing improved diagnostic techniques, intervention and treatment options, and identifying the form of beryllium that is the most important workplace risk factor to control.	Provide better understanding of disease leading to better control, prevention, diagnosis, intervention, and treatment.	1.25	Some early research is complete. Efforts are hampered by lack of an animal model. Diagnostic techniques exist but are intrusive and not sufficiently reliable.	Cellular biology, physical chemistry, pharmacokinetics, biology, biopsy tissue analysis, pulmonary medicine	SC, EH, NIEHS, and NIOSH	Basic

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							Applied
							Epi
							Basic

Needed tools: Health Effects

Animal model and cell line

Develop an animal that models human CBD by contracting the disease after exposure to beryllium.	An animal model is needed to test hypotheses of disease pathways for both skin and lung exposure, determine its natural history, understand genetic components of the susceptibility to disease, and to test intervention and treatment options.	Provide better understanding of disease leading to better control, intervention, and treatment.	0.50	LBL has developed a genetically altered mouse that exhibits beryllium sensitivity. Testings for CBD is needed. Other genes or animals may be needed if CBD does not develop in this mouse.	Genetics, immunology, statistics	SC and NIEHS	Basic
Develop a human cell line that responds to beryllium.	A human cell line is needed to test hypotheses of disease pathways for both skin and lung exposure, determine its natural history, understand genetic components of the susceptibility to disease, and to test intervention and treatment options.	Provide better understanding of disease leading to better control, intervention, and treatment.	0.50		Genetics, immunology, statistics	SC and NIEHS	Basic

Definitions and protocols

Define the natural history of beryllium disease.	Establish standard definitions for sensitization and disease.	Provides essential accuracy and consistency necessary for researching and managing beryllium health effects.	0.05	Some definitions are available in references, but are not widely accepted by clinicians.	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI, NIEHS, and NIOSH	Basic
Establish standard clinical definitions and protocols for determining sensitization and disease.	Establish standard protocols for determining sensitization and disease.	Provides essential accuracy and consistency necessary for researching and managing beryllium health effects.	0.05	Some protocols are available in references but are not widely accepted by clinicians.	Genetics, biology, immunology, statistics, pulmonary medicine, statistics, epidemiology.	SC , EH, NHLBI, NIEHS, and NIOSH	Basic

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							Applied
							Epi
							Basic
Detection in tissue, biomarkers							
Develop in-vitro and in-vivo technologies for detecting beryllium in tissue.	Develop in-vitro and in-vivo technologies for detecting beryllium in tissue.	Needed to conduct research into fate of beryllium in the body. Increase sensitivity of screening workers for beryllium exposure.	0.50		Cellular biology, physical chemistry, pharmacokinetics, biology, biopsy tissue analysis, pulmonary medicine	SC , EH, NHLBI, NIEHS, and NIOSH	Basic
Identify biomarkers of exposure, such as molecules in serum that indicate exposure, sensitivity, disease.	Detect beryllium in tissue or other body components. May require ultra-sensitive analytic methods, such as accelerator mass spectrometry.	Increase sensitivity of screening workers for beryllium exposure. Needed to conduct research into fate of beryllium in the body.	0.50	LLNL reports promising new technology using accelerator mass spectrometry for quantifying femptogram amounts of Be isotopes.	Chemistry, radiochemistry, nuclear physics, industrial hygiene, statistics	NNSA, EH, and NIOSH	Epidemiology
Disease registry							
Develop a nationwide beryllium registry for all sensitized and CBD individuals.	Develop a nationwide beryllium registry for all sensitized and CBD individuals. This may aid in determining the genetic risk factors for increased risk among ethnic populations.	Allow DOE to inform workers of risk factors before the workers are exposed.	0.25		Pulmonary medicine, statistics, epidemiology, industrial hygiene	EH , NHLBI, and NIOSH	Epidemiology
Risk communication							
Determine effective means for communicating beryllium risk.	Determine effective means for communicating beryllium risk so that workers obtain sufficient understanding to make informed decisions concerning employment and medical screening.	Maximize workforce productivity by workers understanding their risks.	0.05	Occupational health risk models are available to evaluate and modify.	Pulmonary physicians, industrial hygienists, ethicists, editors, graphic artists, risk communication specialists.	EH, NNSA, EM	Epidemiology

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							Applied
							Epi
							Basic
Tissue repository							
Develop a nationwide tissue repository (library) of samples obtained from beryllium sensitized and diseased patients.	To have a library available so that all researchers have access for various research projects. Access to tissues currently is limited to those who have patients with sensitization or disease or those who can obtain the tissue through collaboration. This item is designed to allow for any researcher to be able to work on the beryllium problem by providing samples of tissues obtained from sensitized and diseased patients. Bio-specimens also needed from people who were exposed but not sensitized or diseased, and are unexposed.	Improve understanding of disease by increasing the number of researchers who are able to work the problem.	0.50	Funds have been transferred from DOE/EH to NIH/National Heart, Lung, and Blood Institute to establish the repository. Cooperation of clinics and patients is needed.	Blood and tissue medicine.	EH and NHLBI	Epidemiology
Total for All			14.60				